APPENDIX A

OTHER CONSTITUENTS

I. INTRODUCTION

The following is a brief discussion of other constituents in cigarette smoke sometimes referenced by anti-smokers. As stated previously, the vast majority of such constituents, some of which have been identified in "tar," are present in cigarette smoke only in extremely small amounts. As is the case with "tar," nicotine and CO, these minute subfractions of tobacco smoke have not been scientifically proven to cause human disease as they are encountered by the smoker.

II. OTHER CONSTITUENTS

Acetaldehyde

Acetaldehyde is reportedly present in cigarette smoke in minute quantities. It is a chemical compound related to ethanol and is used in the manufacturer of plastics and synthetic rubber. Acetaldehyde is also commonly found in perfume.[1] Exposure to extremely high levels of acetaldehyde has an eye and skin irritant effect, and may be toxic.[2] However, an international research group recently concluded that the data was "inadequate" to support any claim that acetaldehyde causes cancer in humans at any level of exposure.[3]

Acetone

Acetone has been reported to be present in minute quantities in the "vapor phase" of cigarette smoke, i.e., it is not found in "tar" (smoke condensate). It is most commonly encountered either at work or at home in the form of cleaning solvent. It has

also been detected in freeze-dried foods and dried milk. Moreover, acetone is a naturally occurring constituent of human blood and urine.[4]

Acetone is not considered toxic at low levels of exposure, although at higher levels of exposure it can be an eye or skin irritant.[5] One researcher reported that he was unable to produce tumors through the mouse-skin painting method using acetone.[6]

Acrolein

Acrolein has been reported to be present in small quantities in the vapor phase of cigarette smoke. It is also everywhere in the environment as a product of fires, automobile exhaust, and other industrial emissions. Acrolein is also produced by burning foods containing fat, such as grilling a steak.[7] Although at high concentrations acrolein may have a toxic or irritant effect, one recent review of the research conducted regarding acrolein's toxicity or carcinogenicity in humans concluded "there is no evidence to support that acrolein is a human carcinogen."[8]

Ammonia

Ammonia is reportedly detectable in minute amounts in cigarette smoke. It occurs naturally as a part of protein metabolism in man and in virtually all species of animals. Ammonia is widely used as a fertilizer. It is also a common household cleanser.[9] At high concentrations, ammonia can have a strong irritant

effect and cause burns; its pungent odor, of course, is very familiar. One researcher, however, recently noted that:

> The biologic significance of inhaled ammonia in the concentrations generated in mainstream smoke, which are very low, is purely conjectural.[10]

Arsenic

Arsenic is a naturally occurring metal that is drawn into growing tobacco (and other plants) from the soil. It is present also in rocks, water, and virtually all living organisms in concentrations of parts per million and parts per billion. The United States government has estimated that non-smokers generally take in up to 60 micrograms of arsenic per day from various sources; it has also estimated that smokers take in an additional two micrograms of arsenic per pack of cigarettes smoked, thus increasing their daily arsenic intake only marginally.[11] One recent literature review noted that over 99% of the arsenic (and other metals such as lead and cadmium) in tobacco remains in cigarette ash.[12]

Analyses of the literature regarding the relationship between exposure to arsenic and disease have generally been inconclusive. For example, in a recent review of the literature, a researcher characterized "its claimed effects on human smokers as speculative."[13] The 1982 U.S. Surgeon General's Report also noted that "the view that inorganic arsenicals cause cancer of the skin and lung has not been widely accepted. . . ."[14]

Benzene

Benzene has been reported to be present in the vapor phase of cigarette smoke in small quantities. Although benzene has sometimes been suggested as a possible cause of leukemia, leukemia has not been consistently related to cigarette smoking in the various statistical studies that form the primary basis for public health criticism of smoking.[15] The U.S. Surgeon General has also noted that "no dose-response relationship has been established between death rate from leukemia and number of cigarettes smoked."[16]

Benzo(a)pyrene

Benzo(a)pyrene (BaP) is sometimes singled out as a possible human carcinogen because it is a component of the laboratory product "tar;" "tar," as noted above, can produce tumors under the highly artificial conditions involved in animal skin painting experiments. Claims that BaP, and other polycyclic aromatic hydrocarbons (such as dibenzacridine), can cause cancer in humans thus suffer from the same weaknesses as those claims generally directed at "tar."

BaP is formed by the incomplete combustion of organic matter. In addition to cigarette smoke, other sources of BaP in the atmosphere are coal and oil fired power stations, domestic heating, industrial processes and emissions, automobile emissions, and forest fires and volcanic activity. Atmospheric BaP is carried into the soil, the water table, and the ocean through rainfall. Thus, BaP is detectable in fish, meat and vegetables, as well as

in drinking water. Foodstuffs as varied as coconut oil, sardines, and cheese all contain BaP at relatively high levels. Charcoal-grilled meats have been reported to contain particularly high levels of BaP.[17] Two researchers concluded that the BaP concentration in a single charcoal-grilled steak was equivalent to that in the smoke of 600 cigarettes.[18] The daily levels of exposure to BaP simply from breathing the air in some cities has been estimated, by a former U.S. Surgeon General, to be approximately twice as high as that for a cigarette smoker.[19]

Butane

Butane may be present in the vapor phase of cigarette smoke in minute quantities. It occurs in natural gas and is present in the atmosphere as the result of the combustion of gasoline and other petroleum products. Butane is also frequently used as an aerosol propellant. The inhalation of butane has not been demonstrated to produce disease in humans.[20]

Cadmium

Cadmium is a trace "heavy metal" that has been reported to be present in tobacco and in cigarette smoke in certain compound forms. It is used extensively in the production of cadmium-copper alloys and corrosion-resistant coatings. It is found in alkaline batteries, glass, solder, paint pigments and some pesticides and fungicides. The principal sources of cadmium exposure for man are in food, dairy products and drinking water.[21]

It has been estimated that in most countries the average smoker is exposed to approximately the same amount of cadmium daily through smoking as he or she is through diet.[22] Other researchers recently concluded that the amount of cadmium in two packs of cigarettes, even if entirely inhaled, would still be less than would be inspired in two hours of breathing atmospheric cadmium at the maximum safe levels established by the health authorities of several countries.[23]

Cadmium has been identified as a possible tumor promotor under experimental conditions in animals. Three German researchers recently observed, however, that the results of these experiments should not be extrapolated to humans because the doses necessary to induce tumor production corresponded to smoking between 5,000 to 20,000 cigarettes per day.[24] Similarly, a recent review of the literature concerning the claimed carcinogenicity of cadmium noted that "evidence for potential cadmium carcinogenicity in humans in the dosages delivered from smoking is very limited."[25]

Chromium

Chromium is a metal that is reportedly detectable in trace amounts in tobacco. Like the other trace metals in tobacco, it is drawn into the growing plant from the soil. Also like the other metals in tobacco, it is estimated by one researcher that over 99% of the chromium in tobacco remains in cigarette ash and is not transferred into smoke.[26] A group of researchers recently concluded that "[t]here is no indication . . . that the chromium

[in tobacco] goes to the mainstream smoke."[27] (Emphasis added)

Chromium is a naturally occurring element of rock; as rock is weathered into soil, the chromium is transferred into the soil as well. From the soil, chromium is both washed into the oceans, where it is incorporated into the oceanic food-chain, and it is taken up by growing plants and incorporated into the land food-chain. Chromium compounds are also present in the atmosphere as a result of industrial emissions of the burning of organic matter.[28] Food is the principal environmental source of chromium intake by man, with vegetables, unrefined sugar, beef, liver, eggs and animal fats generally having the highest concentrations.[29]

Studies of various illnesses developed by workers in the chromate industry, who were exposed to large concentrations of chromium compounds over many years, have raised concerns about chromium as a possible cause of chronic disease in humans.[30] These studies have been subject to scientific criticism.[31] Given the extremely low level, if any, to which a smoker is exposed to chromium beyond his or her normal dietary and environmental chromium intake, according to one researcher "its role as a potential carcinogen in human smokers is not known."[32]

Hydrogen Cyanide

Hydrogen cyanide (HCN) is also reportedly present in minute amounts in the vapor phase of cigarette smoke. It is produced by the combustion of the amino acids in tobacco. HCN is also generated by the combustion of carbon materials in air, for

example, during home cooking. HCN is used in a variety of industrial processes and is also present in such varied food products as bitter almonds, lima beans, soybeans, apricots, and linseed. It has been detected in certain wines.[33]

A recent study noted that although the HCN level detectable in smokers' blood is slightly elevated after smoking, it is rapidly eliminated from the system.[34] Another reviewer concluded that the effect of HCN in cigarette smoke, if any, on humans "remains to be determined."[35]

Lead

Lead, like the other trace metals reportedly present in tobacco, is drawn from the soil into the growing plant. Also like the other trace metals, one researcher estimated that less than one percent of the lead in the tobacco is transferred to the smoke, with the remainder left in the ash.[36] Lead is present in the air, soil and water. Hence, smokers and non-smokers alike are exposed to and ingest small amounts of lead each day. One research group has estimated that a smoker will ingest five micrograms of lead from a pack of cigarettes; the dietary intake of lead per day, however, has been reported to be much higher.[37]

Numerous health concerns have been expressed regarding exposure to high levels of lead and lead compounds. However, given the very low levels of lead exposure from tobacco, one researcher concluded that "the role of lead as a potential carcinogen for human smokers is not known."[38]

Methanol

Methanol is reported to be present in very small quantities in cigarette smoke as a vapor phase component. It is used in enamels, dyes, stains, cleaning solvents, paint and varnish removers, antifreeze mixtures, and as fuel for internal combustion engines. It is also present in bread, soy sauce and various fruits and vegetables.[39]

Methanol can be a skin and eye irritant in large concentrations. One researcher recently noted, however, that "[c]onsidering the dose of methanol estimated to be toxic to humans (1 g/kg), it is unlikely that a normal human being could ever be exposed to enough of it by inhalation to experience acute toxicity."[40] This scientist also noted that he had been unable to find any studies showing the inhalation of methanol to be carcinogenic.

Naphthalene

Naphthalene is a substance related to benzene. It is reportedly present both in "tar" and in the vapor phase of cigarette smoke in small quantities, and is generated by the combustion of tobacco. Naphthalene is used extensively in the chemical, plastics and dye industries. In the home, it is found frequently in air fresheners, moth balls, varnishes and wood preservatives. Radishes also contain naphthalene.[41] Naphthalene has no conclusive reported carcinogenic effect, although it is sometimes associated with leu-

kemia in animal experiments. As noted above, leukemia has not been consistently statistically associated with cigarette smoking.[42]

Nickel

Nickel, like arsenic, is drawn from the soil into growing tobacco. Also like arsenic, it is estimated that 99% of the nickel in tobacco remains in the ash of a cigarette, and is not transferred to the smoke. The U.S. Surgeon General has concluded that "it is not likely that nickel plays a significant role in the etiology of lung cancer in cigarette smokers. . . ."[43] Other researchers and reviewers have reached the same conclusion.[44]

Nitrogen Oxides

Cigarette smoke reportedly contains nitric oxide (NO), but "very little, if any," nitrous oxide or nitrogen dioxide.[45] The U.S. Surgeon General has noted data showing that both smokers and nonsmokers maintain "a consistently low level" of NO in their blood and has suggested that the "lack of a significant difference" between the two groups indicates that NO from external sources "appears to have little effect" on the amount found in the blood.[46]

Nitrosamines

Nitrosamines reportedly are detectable in both "tar" and in the vapor phase component of cigarette smoke. The presence of nitrosamines in cigarette smoke is often the subject of public comment by anti-smoking advocates because, under experimental con-

ditions, certain nitrosamine compounds can produce tumors in laboratory animals. As two reviewers of the literature noted, however, "direct epidemiologic evidence that would associate nitrosamines with human cancer is very limited."[47] Another recent reviewer suggested that:

> The role of nitrosamines in the pathogenesis of human lung cancers is theoretical, and it is yet to be shown conclusively that any specific N-nitroso compound causes human cancer.[48]

Even the U.S. Surgeon General has stated that there is "a lack of direct evidence" that the nitrosamines specific to tobacco have any proven health effect on smokers.[49]

The components of nitrosamines -- nitrates, nitrites and amines -- are naturally occurring substances. Hence, nitrosamines are found in soil, air, water and food. Beer and scotch whiskey have recently been determined to contain dimethylnitrosamine.[50] Foods often prepared with nitrites (used as a preservative) include ham, sausages, bacon, luncheon meats and frankfurters; seafood and cheese also often contain nitrosamines.[51]

Phenol

Phenol is reported to be present in minute quantities in cigarette smoke and is detectable in "tar." It has a variety of industrial uses, including the manufacture of perfumes, plastics and fertilizers. Phenol occurs naturally in animal tissues; the consumption of meat has been identified as the primary source of human exposure to phenol. It is also present in drinking water.[52]

Two reviewers of the literature concluded that "[t]here is no specific evidence of human cancer attributable to phenol or related compounds. . . ."[53] A group of researchers likewise reported that phenol is not present in cigarette smoke at high enough concentrations to cause disease in smokers.[54]

Polonium-210

Polonium-210 is a radioactive element that has been reported to be present in trace amounts in tobacco and cigarette smoke. It is also present in the atmosphere and in soil -- both as a part of the earth's natural background radiation and as a result of nuclear testing -- from which it is presumably drawn into growing tobacco. Smoking critics often cite the presence of polonium-210 in smoke as significant because it, along with most other radioactive materials, can have adverse health effects in humans and in animals if the exposure is of sufficient intensity. Even the U.S. Surgeon General, however, has questioned the significance of polonium-210 to lung cancer in humans.[55] Other researchers have disputed the conclusion drawn by some scientists that polonium-210 accumulates in the lung tissue of smokers.[56] Additional researchers discount the claimed risk to smokers of inhaled polonium, noting the extraordinarily minute quantities at which it is present.[57]

Toluene

Toluene is reported to be a constituent of the vapor phase component of cigarette smoke. It is present in the atmosphere as a result of industrial emissions, automobile emissions, and gasoline evaporation. Exposures at home include inks, dyes, and perfumes.[58] Although it is an eye and skin irritant at low levels and concentrations, toluene has not been reported to be toxic or to cause chronic disease in humans at those levels.[59]

Urethane

Urethane (ethyl carbamate) has been reported to be present in cigarette smoke in very small amounts. It has been widely used in the plastics and textile industries. It is also used in a variety of agricultural chemicals, pesticides, fungicides, and in some therapeutic drugs. Urethane is a natural by-product of fermentation, and is found in wines, distilled spirits, and beer, as well as in fermented food products such as cheese, yogurt and soy sauce.[60] The U.S. Surgeon General has conceded that urethane, although possibly an animal carcinogen, is not present in cigarette smoke in sufficient quantities to cause cancer in smokers.[61]

Vinyl Chloride

Vinyl chloride is reportedly present in minute amounts in the vapor phase of cigarette smoke. Although it is a gas, it is detectable in various food products such as honey, butter and tomato ketchup. It is also present in some wines.[62] Vinyl chloride

is also used in the manufacture of plastics.[63]

Vinyl chloride has been reported to have toxic and carcinogenic effects in animals at high concentrations; a similar effect on humans has been suggested. One group of oncologists, however, although subscribing to the general theory that smoking causes cancer, conceded that:

> Based on human data and results from animal studies, it appears to us that the[] minute amounts of [vinyl chloride in cigarette smoke] will not contribute to a measurable degree to the carcinogenic activity of tobacco smoke.[64]

This conclusion was echoed by a recent literature reviewer, who concluded that vinyl chloride is present in cigarette smoke "apparently at levels too low to be considered a carcinogen or fibrosis-inducing agent."[65]

REFERENCES

1. "Hazardous Materials: Acetaldehyde," Dangerous Properties of Industrial Materials Report 9(6): 30-45, 1989.

2. "Hazardous Materials: Acetaldehyde," Dangerous Properties of Industrial Materials Report 9(6): 30-45, 1989.

Brabec, M.J., "Chapter Thirty-Seven. Aldehydes and Acetals." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 2629-2669 (see particularly 2633, 2646), 1982.

3. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, "Acetaldehyde (Group 2B)," IARC Monographs On the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42, Supplement 7, 77-78 (at 77), 1987.

4. Krasavage, W.J., O'Donoghue, J.L., and DiVincenzo, G.D., "Ketones." In: Chapter Fifty-Six. Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 4709-4800 (see particularly 4726), 1982.

Kayaert, G., Tobback, P., Maes, E., Flink, J. and Karel, M., "Retention of Volatile Organic Compounds in a Complex Freeze-Dried Food Gel," Journal of Food Technology 10(1): 11-18, 1975.

Maier, H.G., "Zur Bindung flüchtiger Aromastoffe an Lebensmittel. VI. Mitteilung. Einfache Ketone (Binding of Volatile Aroma Constituents in Foods. VI. Continuation. Simple Ketones)," Zeitschrift Für Lebensmittel -Untersuchung und -Forschung 149(2): 65-69, 1972. English Summary.

5. Krasavage, W.J., O'Donoghue, J.L., and DiVincenzo, G.D., "Ketones." In: Chapter Fifty-Six. Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 4709-4800 (see particularly 4724-4726), 1982.

6. Bock, F.G., Swain, A.P. and Stedman, R.L., "Composition Studies on Tobacco. XLI. Carcinogenesis Assay of Subfractions of the Neutral Fraction of Cigarette Smoke Condensate," Journal of the National Cancer Institute 44(6): 1305-1310, 970.

7. Beauchamp, R.O., Andjelkovich, D.A., Kligerman, A.D., Morgan, K.T. and Heck, H.d'A., "A Critical Review of the Literature on

Acrolein Toxicity," CRC Critical Reviews in Toxicology 14(4): 309-380, 1985.

Sakata, T., Smith, R.A., Garland, E.M. and Cohen, S.M., "Rat Urinary Bladder Epithelial Lesions Induced by Acrolein," Journal of Environmental Pathology, Toxicology, and Oncology 9(2): 159-169, 1989.

Feron, V.J., and Kruysse, A., "Effects of Exposure to Acrolein Vapor in Hamsters Simultaneously Treated with Benzo[a]pyrene or Diethylnitrosamine," Journal of Toxicology and Environmental Health 3(3): 379-394, 1977.

8. Beauchamp, R.O., Andjelkovich, D.A., Kligerman, A.D., Morgan, K.T. and Heck, H.d'A., "A Critical Review of the Literature on Acrolein Toxicity," CRC Critical Reviews in Toxicology 14(4): 309-380 (at 342), 1985.

9. Wands, R.C., "Chapter Forty-One. Alkaline Materials: 1. Ammonia, NH_3, Ammonium Hydroxide, NH_4OH, and Ammonium Salts." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 3045-3052, 3067-3069, 1982.

10. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 316), October, 1989.

11. Stokinger, H.E., "Chapter 29. The Metals: 3. Arsenic, As." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 1517-1531, 1982.

Jacobson-Kram, D., Mushak, P., Piscator, M., Sivulka, D.J., Chu, M., Gibb, H.J., Thorslund, T.W. and Crump, K.S., "9. Human Health Risk Assessment for Arsenic," Health Assessment Document for Inorganic Arsenic: Final Report, Washington, D.C., United States Environmental Protection Agency, Office of Health and Environmental Assessment, EPA-600/8-83-021F, 1-11 (at particularly 3-4), March, 1984.

National Academy of Sciences, Committee on Medical and Biologic Effects of Environmental Pollutants, "2. Chemistry of Arsenic." In: Medical and Biologic Effects of Environmental Pollutants: Arsenic. Washington, D.C., National Academy of Sciences, 4-15 (see particularly 4), 1977.

12. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (see particularly 313), October, 1989.

13. Huber, G.L, "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 313), October, 1989.

14. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, "Part III. Mechanisms of Carcinogenesis: Experimental Carcinogenesis With Tobacco Smoke," The Health Consequences of Smoking: Cancer. A Report of the Surgeon General: 1982, DHHS Publication No. (PHS) 82-50179, Washington, D.C., U.S. Government Printing Office, 181-235 (at 211), 1982.

15. Huber, G.L., "Physical, Chemical, and Biological Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (see particularly 312, 316), October, 1989.

16. U.S. Department of Health, Education, and Welfare, Public Health Service, Office on Smoking and Health, "Chapter 14. Constituents of Tobacco Smoke: Benzenes and Naphthalenes," Smoking and Health. A Report of the Surgeon General, DHEW Publication No. (PHS) 79-50066, Washington, D.C., U.S. Government Printing Office, 49, 51 (at 51), 1979.

17. Osborne, M.R. and Crosby, N.T., "Occurrence of Benzopyrenes in the Environment." In: Benzopyrenes. M.M. Coombs, J. Ashby, R.F. Newbold and H. Baxter (eds.). Cambridge, Cambridge University Press, Chapter 17, 301-316, 1987.

Sandmeyer, E.E., "Chapter Forty-Seven. Aromatic Hydrocarbons. 4. Tri- and Polynuclear Ring Systems." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 3253-3431 (see particularly 3345), 1982.

18. Lijinsky, W. and Shubik, P., "Benzo(a)pyrene and Other Polynuclear Hydrocarbons in Charcoal-Broiled Meat," Science 145(2): 53-55, 1964.

19. Burney, L.E., "Governmental Responsibilities in Environmental Health," Public Health Reports 76(4): 291-295 (see particularly 293) April, 1961.

20. Sandmeyer, E.E., "Chapter Forty-Five. Aliphatic Hydrocarbons. 1.5. Butanes." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 3182-3183, 1982.

Beall, J.R. and Ulsamer, A.G., "Toxicity of Volatile Organic Compounds Present Indoors," Bulletin of The New York Academy

of Medicine 57(10): 978-997 (see particularly 980), December, 1981.

21. Stokinger, H.E., "Chapter Twenty-Nine. The Metals: 7. Cadmium, Cd." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 1563-1582, 1982.

Kendrey, G. and Roe, F.J.C., "Cadmium Toxicology," The Lancet, 1206-1207, June 14, 1969.

Gloag, D., "Contamination of Food: Mycotoxins and Metals," British Medical Journal 282(6267): 879-882, March 14, 1981.

22. Lewis, G.P., Jusko, W.J., Coughlin, L.L., and Hartz, S., "Contribution of Cigarette Smoking to Cadmium Accumulation in Man," The Lancet 1(7745): 291-292, February 5, 1972.

Elinder, C.G., Kjellstrom, T., Lind, B., Linnman, L., Piscator, M. and Sundstedt, K., "Cadmium Exposure From Smoking Cigarettes: Variations With Time and Country Where Purchased," Environmental Research 32(1): 220-227, October, 1983.

Scherer, G. and Barkemeyer, H., "Cadmium Concentrations in Tobacco and Tobacco Smoke," Ecotoxicology and Environmental Safety 7(1): 71-78, February, 1983.

Westcott, D.T. and Spincer, D., "The Cadmium, Nickel and Lead Content of Tobacco and Cigarette Smoke," Beiträge zur Tabakforschung 7(4): 217-221, April, 1974.

23. Hennigar, G.R. and Gross, P., "Chapter 5: Drug and Chemical Injury -- Environmental Pathology." In: Anderson's Pathology. J.M. Kissane (ed.). St. Louis, C. V. Mosby Company, Volume 1, 147-238 (see particularly 207), 1985.

24. Schmidt, J.A., Fischbach, E.-D. and Burkart, F., "Cadmium-Untersuchungen im Bereich von Umwelt-, Boden- und Sorteneinflüssen bei Tabak sowie der Cadmium-Übergang in den Zigarettenrauch (A Study of the Influences of Environment, Soil and Varieties on Cadmium Contents in Tobacco and of Cadmium Transfer into Cigarette Smoke)," Zeitschrift für Lebensmittel -Untersuchung und -Forschung 180(4): 306-311, 1985. English Summary and Translation.

25. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 313), October, 1989.

26. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars

in Respiratory Medicine 10(4): 297-332 (see particularly 313), October, 1989.

27. Fan, A.M. and Harding-Borlow, I., "Chromium." In: Advances in Modern Environmental Toxicology. Volume XI. Genotoxic and Carcinogenic Metals: Environmental and Occupational Occurrence and Exposure, L. Fishbein, A. Furst and M.A. Mehlman (eds.). Princeton, Princeton Scientific Publishing Co., Inc., 87-125 (at 89), 1987.

28. WHO Expert Committee on International Programme on Chemical Safety (IPCS), "3. Sources in the Environment, Environmental Transport and Distribution," Environmental Health Criteria 61: Chromium, Geneva, World Health Organization, 32-41, 1988.

Fan, A.M. and Harding-Borlow, I., "Chromium." In: Advances in Modern Environmental Toxicology. Volume XI. Genotoxic and Carcinogenic Metals: Environmental and Occupational Occurrence and Exposure, L. Fishbein, A. Furst and M.A. Mehlman (eds.). Princeton, Princeton Scientific Publishing Co., Inc., 87-125, 1987.

29. Fan, A.M. and Harding-Borlow, I., "Chromium." In: Advances in Modern Environmental Toxicology. Volume XI. Genotoxic and Carcinogenic Metals: Environmental and Occupational Occurrence and Exposure, L. Fishbein, A. Furst and M.A. Mehlman (eds.). Princeton, Princeton Scientific Publishing Co., Inc., 87-125, 1987.

30. Stokinger, H.E., "Chapter Twenty-Nine: The Metals. Section 9, Chromium, Cr." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 1589-1605 (see particularly 1601), 1981.

31. Gerhardsson, L., Wester, P.O., Nordberg, G.F. and Brune, D., "Chromium, Cobalt and Lanthanum in Lung, Liver and Kidney Tissue from Deceased Smelter Workers," Science of the Total Environment 37 (2/3): 233-246 (see particularly 242), August 1, 1984.

32. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 313), October, 1989.

33. Hartung, R., "Chapter Fifty-Eight. Cyanides and Nitriles. 2. Cyanides. 2.1 Hydrogen Cyanide." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 4850-4853 (see particularly 4850), 1982.

Honig, D.H., Hockridge, M.E., Gould, R.M. and Rackis J.J., "Determination of Cyanide in Soybeans and Soybean Products," Journal of Agricultural and Food Chemistry 31(2): 272-275, 1983.

Misselhorn, K. and Adam, R., "On The Cyanide Contents in Stone Fruit Products," Branntweinwirtschaft 116(4): 45-50, 1976. English Abstract.

Askar, A. and Morad, M.M., "Lebensmittelvergiftung. 1. Toxine in natürlichen Lebensmitteln (Food Poisoning. 1. Toxins in Natural Foodstuffs)," Alimenta 19: 59-66, 1980. English Summary.

34. Lundquist, P., Rosling, H., Sörbo, B. and Tibbling, L, "Cyanide Concentrations in Blood After Cigarette Smoking, as Determined by a Sensitive Fluorimetric Method," Clinical Chemistry 33(7): 1228-1230, 1987.

35. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 315), October, 1989.

36. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (see particularly 313), October, 1989.

37. IARC Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, "Lead and Lead Compounds." In: IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Metals and Metallic Compounds, Volume 23. Lyon, International Agency for Research on Cancer, 325-416 (see particularly 345, 350-351), 1980.

38. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 313), October, 1989.

39. Rowe, V.K. and McCollister, S.B., "Chapter Fifty-Six. Alcohols. 2. Methanol." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 4528-4541, 1982.

Isshiki, K., "Analysis of Methyl and Ethyl Alcohols in Foods and Assessment of Dietary Intake Levels," Shokuhin Eiseigaku Zasshi (Journal of the Food Hygienic Society of Japan) 26(1): 39-45, 1985. English Abstract.

40. Marnett, L.J., "Health Effects of Aldehydes and Alcohols in Mobile Source Emissions." In: Air Pollution, The Automobile and Public Health. Washington, D.C., National Academy Press, 579-603 (at 587), 1988.

41. Sandmeyer, E.E., "Chapter Forty-Seven. Aromatic Hydrocarbons. 3. Dinuclear Systems. 3.1 Naphthalene." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 3333-3343, 3400-3431, 1982.

42. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (see particularly 312), October, 1989.

43. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, "Part III. Mechanisms of Carcinogenesis: Experimental Carcinogenesis With Tobacco Smoke," The Health Consequences of Smoking: Cancer. A Report of the Surgeon General: 1982, DHHS Publication No. (PHS) 82-50179, Washington, D.C., U.S. Government Printing Office, 181-235 (at 211), 1982.

44. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (see particularly 313), October, 1989.

Wynder, E.L. and Hoffmann, D., Tobacco and Tobacco Smoke: Studies in Experimental Carcinogenesis, New York, Academic Press Inc., 493, 498, 627-628, 1967.

45. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 315), 1989.

46. U.S. Department of Health, Education, and Welfare, Public Health Service, Office on Smoking and Health, "14. Constituents of Tobacco Smoke: Toxicity of Specific Smoke Components," Smoking and Health. A Report of the Surgeon General, DHEW Publication No. (PHS) 79-50066, Washington, D.C., U.S. Government Printing Office, 78-84 (at 80), 1979.

47. Reinhardt, C.F. and Brittelli, M.R., "Chapter Thirty-Eight. Heterocyclic and Miscellaneous Nitrogen Compounds. 3.2.3. Dimethylnitrosamine." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 2286-2789 (at 2786), 1982.

48. Huber, G.L., "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 311), October, 1989.

49. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, "Part III. Mechanisms of Carcinogenesis: Experimental Carcinogenesis With Tobacco Smoke," The Health Consequences of Smoking: Cancer. A Report of the Surgeon General: 1982, DHHS Publication No. (PHS) 82-50179, Washington, D.C., U.S. Government Printing Office, 181-235 (at 200), 1982.

50. Reinhardt, C.F. and Brittelli, M.R., "Chapter Thirty-Eight. Heterocyclic and Miscellaneous Nitrogen Compounds. 3.2.3. Dimethylnitrosamine." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 2286-2789, 1982.

51. Fishbein, L., "Overview of Some Aspects of Occurrence, Formation and Analysis of Nitrosamines," Science of the Total Environment 13(2): 157-188, 1979.

Pensabene, J., Fiddler, W., Doerr, R.C., Lakritz, L. and Wasserman, A.E., "Formation of Dimethylnitrosamine From Commercial Lecithin and its Components in a Model System," Journal of Agricultural and Food Chemistry 23(5): 979-980, 1975.

Sen, N.P., Smith, D.C., Schwinghamer, L. and Marleau, J.J., "Food Additives: Dimethylnitrosamine and Other N-Nitrosamines in Foods," Journal of the Association of Official Analytical Chemists 52(1): 47-52, 1969.

52. Deichmann, W.B. and Keplinger, M.L., "Chapter Thirty-Six. Phenols and Phenolic Compounds. 1. Phenol." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 2567-2584, 1982.

Babich, H. and Davis, D.L., "Phenol: A Review of Environmental and Health Risks," Regulatory Toxicology and Pharmacology 1(1): 90-109 (see particularly 90, 103), 1981.

53. Deichmann, W.B. and Keplinger, M.L., "Chapter Thirty-Six. Phenols and Phenolic Compounds. 1. Phenol." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 2567-2584 (at 2583-2584), 1982.

54. Kensler, C.J., Battista, S.P. and Thayer, P.S., "19. Animal Models for the Study of Tobacco Carcinogenesis." In: Human

Epidemiology and Animal Laboratory Correlations in Chemical Carcinogenesis. Frederick Coulston and Philippe Shubik (eds.). Norwood, New Jersey, Ablex Publishing Corporation, 341-357 (see particularly 351), 1980.

55. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, "Part III. Mechanisms of Carcinogenesis: Experimental Carcinogenesis With Tobacco Smoke," The Health Consequences of Smoking: Cancer. A Report of the Surgeon General: 1982, DHHS Publication No. (PHS) 82-50179, Washington, D.C., U.S. Government Printing Office, 181-235 (see particularly 190, 210), 1982.

U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, "Section 3. Cancer," The Health Consequences of Smoking: The Changing Cigarette. A Report of the Surgeon General, DHHS Publication No. (PHS) 81-50156, Washington, D.C., U.S. Government Printing Office, 75-109 (see particularly 94), 1981.

56. Robertson, G.B. and Rogers, A.W., "An Autoradiographic Search for Radioactive Particles in the Lungs of Cigarette Smokers," Archives of Environmental Health 35(2): 117-122, March/April, 1980.

57. Cohen, B.S., Eisenbud, M. and Harley, N.H., "Measurement of the Alpha-Radioactivity on the Mucosal Surface of the Human Bronchial Tree," Health Physics 39(4): 619-632, 1980.

Harley, N.H., Cohen, B.S. and Tso, T.C., "Polonium-210: A Questionable Risk Factor in Smoking-Related Carcinogenesis." In: Banbury Report 3: A Safe Cigarette? G.B. Gori and F.G. Bock (eds.). Cold Spring Harbor, New York, Cold Spring Harbor Laboratory, 93-104, 1980.

58. Sandmeyer, E.E., "Chapter Forty-Seven. Aromatic Hydrocarbons. 1.3. Toluene." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F. E. Clayton (eds.). New York, John Wiley & Sons, 3283-3291, 3400-3431, 1982.

59. Gibson, J.E. and Hardisty, J.F., "Chronic Toxicity and Oncogenicity Bioassay of Inhaled Toluene In Fischer-344 Rats," Fundamental and Applied Toxicology 3: 315-319, July/August, 1983.

Häsänen, E., Karlsson, V., Leppämaki, E. and Juhala, M., "Short Communication: Benzene, Toluene and Xylene Concentrations in Car Exhausts and in City Air," Atmospheric Environment 15(9): 1755-1757, 1981.

Carpenter, C.P., Geary, D.L. Jr., Myers, R.C., Nachreiner, D.J., Sullivan, L.J. and King, J.M., "Petroleum Hydrocarbon Toxicity Studies. XIII. Animal and Human Response to Vapors of Toluene Concentrate," Toxicology and Applied Pharmacology 36(3): 473-490, 1976.

60. Canas, B.J., Havery, D.C., Robinson, L.R., Sullivan, M.P., Joe, F.L., and Diachenko, G.W., "Ethyl Carbamate Levels in Selected Fermented Foods and Beverages," Journal of the Association of Official Analytical Chemists 72(6): 873-876, 1989.

Ingledew, W.M., Magnus, C.A., and Patterson J.R., "Yeast Foods and Ethyl Carbamate Formation in Wine," American Journal of Enology Viticulture 38(4): 332-335, 1987.

Mossoba, M.M., Chen, J.T., Brumley, W.C., and Page, S.W., "Application of Gas Chromatography/Matrix Isolation/Fourier Transform Infrared Spectrometry to the Determination of Ethyl Carbamate in Alcoholic Beverages and Foods," Analytical Chemistry 60(9): 945-948, May 1, 1988.

61. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, "Part III. Mechanisms of Carcinogenesis: Experimental Carcinogenesis With Tobacco Smoke," The Health Consequences of Smoking: Cancer. A Report of the Surgeon General: 1982, DHHS Publication No. (PHS) 82-50179, Washington, D.C., U.S. Government Printing Office, 181-235 (see particularly 194), 1982.

62. Squirrell, D.C.M. and Thain, W., "Method 8 -- Determination of Vinyl Chloride in Foodstuffs by Head-Space Sampling Gas Chromatography." In: Environmental Carcinogens Selected Methods of Analysis. Volume 2 - Methods for the Measurement of Vinyl Chloride in Poly (Vinyl Chloride), Air, Water and Foodstuffs. H. Egan and W. Davis (eds.). Lyon, International Agency for Research on Cancer, IARC Scientific Publications, Monograph No. 22, 113-120 (see particularly p. 113), 1978.

Albanus A.L., Gawell, B.-M., Larsson, B. and Slorach, S.A., "Sänkt maximigräns för vinylklorid i livsmedel (Reduced Maximum Tolerance for Vinyl Chloride in Foods)," Var Föda 31(3): 161-168, March, 1979. English Summary.

63. Torkelson, T.R. and V.K. Rowe, "Chapter Forty-Eight. Halogenated Aliphatic Hydrocarbons. 3. Unsaturated Halogenated Hydrocarbons. 3.1. Vinyl Chloride." In: Patty's Industrial Hygiene and Toxicology. Third Revised Edition. G.D. Clayton and F.E. Clayton (eds.). New York, John Wiley & Sons, 3537-3542, 3595-3596 (see particularly 3537), 1982.

64. Hoffmann, D., Patrianakos, C. and Brunnemann, K.D., "Chromatographic Determination of Vinyl Chloride in Tobacco Smoke," Analytical Chemistry 48(1): 47-50 (at 50), January, 1976.

65. Huber, G.L, "Physical, Chemical, and Biologic Properties of Tobacco, Cigarette Smoke, and Other Tobacco Products," Seminars in Respiratory Medicine 10(4): 297-332 (at 316), October, 1989.